

PCT COOPERATION TREATY

PCT

NOTIFICATION OF THE RECORDING
OF A CHANGE(PCT Rule 92bis.1 and
Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

ROBINSON, J., Christopher
Smart & Biggar
Suite 2200
650 West Georgia Street
Box 11560
Vancouver, British Columbia V6B 4N8
CANADA

Date of mailing (day/month/year) 01 February 2001 (01.02.01)	IMPORTANT NOTIFICATION
Applicant's or agent's file reference 80021-205	
International application No. PCT/CA00/00663	International filing date (day/month/year) 07 June 2000 (07.06.00)

1. The following indications appeared on record concerning:		
<input checked="" type="checkbox"/> the applicant	<input checked="" type="checkbox"/> the inventor	<input type="checkbox"/> the agent <input type="checkbox"/> the common representative
Name and Address	State of Nationality	State of Residence
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	
2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:		
<input checked="" type="checkbox"/> the person	<input checked="" type="checkbox"/> the name	<input checked="" type="checkbox"/> the address <input checked="" type="checkbox"/> the nationality <input checked="" type="checkbox"/> the residence
Name and Address GRANT, Jason, Robert Suite 902 950 Cambie Street Vancouver, British Columbia V6B 5X5 Canada	State of Nationality CA	State of Residence CA
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	
3. Further observations, if necessary: Please note that GRANT, Jason, Robert should be included on the Records as an additional applicant and inventor for the United States of America (US) only.		
4. A copy of this notification has been sent to:		
<input checked="" type="checkbox"/> the receiving Office	<input checked="" type="checkbox"/> the designated Offices concerned	
<input type="checkbox"/> the International Searching Authority	<input type="checkbox"/> the elected Offices concerned	
<input type="checkbox"/> the International Preliminary Examining Authority	<input type="checkbox"/> other:	

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer F. Baechler Telephone No.: (41-22) 338.83.38
---	---

PCT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner
 US Department of Commerce
 United States Patent and Trademark
 Office, PCT
 2011 South Clark Place Room
 CP2/5C24
 Arlington, VA 22202
 ETATS-UNIS D'AMERIQUE
 in its capacity as elected Office

Date of mailing (day/month/year) 20 February 2001 (20.02.01)	
International application No. PCT/CA00/00663	Applicant's or agent's file reference 80021-205
International filing date (day/month/year) 07 June 2000 (07.06.00)	Priority date (day/month/year) 07 June 1999 (07.06.99)
Applicant MOISE, Alexandru, R. et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:

05 January 2001 (05.01.01)

☐ in a notice effecting later election filed with the International Bureau on:
2. The election ☒ was
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer F. Baechler Telephone No.: (41-22) 338.83.38
---	---

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 80021-205	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/CA00/00663	International filing date (day/month/year) 07/06/2000	Priority date (day/month/year) 07/06/1999
International Patent Classification (IPC) or national classification and IPC C12N15/34		
Applicant THE UNIVERSITY OF BRITISH COLUMBIA		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.



2. This REPORT consists of a total of 7 sheets, including this cover sheet.

- ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 05/01/2001	Date of completion of this report 07.09.2001
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Wimmer, G Telephone No. +49 89 2399 7347 

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/CA00/00663

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, pages:

1-4,6-20 as originally filed

5 as received on 08/01/2001 with letter of 04/01/2001

Claims, No.:

1-17 as originally filed

Drawings, sheets:

1/2,2/2 as originally filed

Sequence listing part of the description, pages:

1-2 (SEQ ID NOs 1-6), as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☒ furnished subsequently to this Authority in written form.
- ☒ furnished subsequently to this Authority in computer readable form.
- ☒ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☒ The statement that the information recorded in computer readable form is identical to the written sequence

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/CA00/00663

listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application.
- ☒ claims Nos. 1-3, 5-7, 12 with respect to industrial applicability.

because:

- ☒ the said international application, or the said claims Nos. 1-3, 5-7, 12 relate to the following subject matter which does not require an international preliminary examination (*specify*):
see separate sheet
- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for the said claims Nos. .

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

- ☐ the written form has not been furnished or does not comply with the standard.
- ☐ the computer readable form has not been furnished or does not comply with the standard.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/CA00/00663

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-8, 12-17
	No:	Claims	9-11
Inventive step (IS)	Yes:	Claims	1-8, 12-17
	No:	Claims	9-11
Industrial applicability (IA)	Yes:	Claims	4, 8-11, 13-17
	No:	Claims	

2. Citations and explanations **see separate sheet**

80021-205

January 4, 2001

COURIER

European Patent Office
Erhardstrasse 27
D-80331 Munchen 2
Germany

Attn: International Preliminary Examining Authority

Dear Sirs:

RE: Patent Cooperation Treaty Application Serial No. PCT/CA00/00663

International Filing Date: June 7, 2000

Earliest Priority Date: June 7, 1999

Demand for Chapter II due: January 7, 2001

**Title: APOPTOSIS INHIBITION BY
ADENOVIRUS E3/6.7K**

Applicant: The University of British Columbia

This is a request for an amendment under Article 34. Please make the following amendments.

In the Description:

Replace page 5 presently on file with the enclosed replacement page.

Remarks:

This amendment corrects a clerical error in the sequence identification numbers set out at page 5, line 13. In the pag presently on file, the sequences ref rred to at that line are indicated as being numbers 4 & 5. However, sequence identification number 4 had

European Patent Office
Our Ref. #80021-205

2

January 4, 2001

already been assigned (see page 5, line 7). Accordingly, the sequence identification numbers at line 13 of page 5 have been amended to read numbers 4 & 5.

We look forward to examination of this application.

Yours very truly,
SMART & BIGGAR

J. Christopher Robinson

JCR/gmk

Enc. Replacement page 5

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 Nucleic acid sequence showing the alignment of the naturally occurring nucleic acid sequence (SEQ ID NO: 1), which is capable of encoding a E3/6.7K protein corresponding to that of Adenovirus serotype Ad2 wild-type (Wt.), and the Polymerase Chain Reaction (PCR) nucleic acid product expected (SEQ ID NO: 2) when the forward primer (FP - SEQ ID NO: 3) and reverse primer (RP - SEQ ID NO: 4) are used to amplify the wild-type sequence (Wt.). Start codons are underlined. The nucleic acids shown in bold in the forward primer (FP) represent a modification to provide a Kozak consensus sequence. The nucleic acids shown in bold in the reverse primer (RP) is a modified stop codon to enhance translation.

Figure 2 Amino acid sequence showing the alignment of the E3/6.7K protein amino sequences from the Ad2 (SEQ ID NO: 5) and Ad5 (SEQ ID NO: 6) Adenovirus serotypes. The Ad 2 E3/6.7K amino acid sequence is 61 amino acids in length and the Ad5 E3/6.7K amino acid sequence is 63 amino acids in length.

DETAILED DESCRIPTION OF THE INVENTION

As used herein for description of this invention, the terms E3/6.7K protein and E3/6.7K polypeptide include: a protein or fragment thereof encoded by a nucleic acid as depicted in Figure 1; a Ad2 or Ad5 adenovirus serotype protein or fragment thereof as depicted in Figure 2; or a protein having at least 70% similarity as defined by a Basic Blast search using default parameters to the Ad2 or Ad5 proteins depicted in Figure 2. The Ad5 protein is actually about 7.1K.

Modulation of apoptosis, including inhibition of apoptosis or rescue of a cell from apoptosis may be determined by various methods known in the art, including assays which directly measure apoptosis or which measure the activity of TNF- α , such as those described herein.

Gene Therapy Methods. The isolated nucleic acid molecule depicted in Figure 1, a nucleic acid molecule encoding an E3/6.7K protein as defined herein or a nucleic acid molecule complementary to those described above, may be incorporated into a vector suitable

Re Item III

Non-establishment of opinion.

Claims 1-3, 5-7 and 12 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

Re Item V

Reasoned statement under Art. 35(2) PCT with regard to novelty, inventive step or industrial applicability.

- 1) Reference is made to the following documents (the document numbering corresponds to their order of citation in the international search report):

D1: WO 99 02658 A (SAINT LOUIS UNIVERSITY) 21 January 1999 (1999-01-21)

D4: ELSING ANDREAS ET AL: 'The adenovirus E3/10.4K-14.5k proteins down-modulate the apoptosis receptor Fas/Apo-1 by inducing its internalization.' PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES, vol. 95, no. 17, 18 August 1998 (1998-08-18), pages 10072-10077, XP002151270 Aug. 18, 1998 ISSN: 0027-8424

D6: WILSON-RAWLS JEANNE ET AL: 'The signal-anchor domain of adenovirus E3-6.7K, a type III integral membrane protein, can direct adenovirus E3-gp19k, a type I integral membrane protein, into the membrane of the endoplasmic reticulum.' VIROLOGY, vol. 201, no. 1, 1994, pages 66-76, XP002151272 ISSN: 0042-6822 cited in the application

Novelty under Art. 33(2) PCT.

- 2) Numerous experiments on the E3 region of adenovirus, and also of the 6.7K polypeptide, have been performed in the prior art. In the course of this, several constructs have been created which fall under the terms of claims 9-11. For example, document D1 describes the creation of mutant replication-deficient viruses, in which the Ad2 E3 genes have been placed under the control of a CMV promoter, flanked by Ad5 sequences (pgs. 32/33). As another example, document D6 and references cited therein (Wold 1986) cites the use of adenoviruses with contain modifications to the 6.7K gene.

As a consequence, claims 9-11 cannot be acknowledged to be novel.

- 3) No document of the prior art suggests the use of the E3/6.7K protein in a medical application. Also, E3/6.7K was never implied to have a function in apoptotic pathways.

Therefore, claims 1-8 and 12-17 are viewed to be novel.

Inventive Step under Art. 33(3) PCT.

- 4) Despite extensive examination of the adenoviral E3 locus in general, and the 6.7K protein in particular, the prior art does not imply a role of the E3/6.7K protein in apoptosis. In fact, document D4 identifies the E3/10.4K and 14.5K proteins to mediate down-regulation of Fas, but states that cells transfected with constructs encoding other E3 proteins (12.5K, 6.7K, 19K, and 11K) appear to have normal levels of Fas, actually leading the skilled person away from the invention of the application.

An inventive step is therefore acknowledged for subject-matter of claims 1-8 and 12-17.

Industrial Applicability under Art. 33(4) PCT.

- 5) For the assessment of the present claims 1-3, 5-7 and 12 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 Nucleic acid sequence showing the alignment of the naturally occurring nucleic acid sequence (SEQ ID NO: 1), which is capable of encoding a E3/6.7K protein corresponding to that of Adenovirus serotype Ad2 wild-type (Wt.), and the Polymerase Chain Reaction (PCR) nucleic acid product expected (SEQ ID NO: 2) when the forward primer (FP - SEQ ID NO: 3) and reverse primer (RP - SEQ ID NO: 4) are used to amplify the wild-type sequence (Wt.). Start codons are underlined. The nucleic acids shown in bold in the forward primer (FP) represent a modification to provide a Kozak consensus sequence. The nucleic acids shown in bold in the reverse primer (RP) is a modified stop codon to enhance translation.

Figure 2 Amino acid sequence showing the alignment of the E3/6.7K protein amino sequences from the Ad2 (SEQ ID NO: 5) and Ad5 (SEQ ID NO: 6) Adenovirus serotypes. The Ad 2 E3/6.7K amino acid sequence is 61 amino acids in length and the Ad5 E3/6.7K amino acid sequence is 63 amino acids in length.

DETAILED DESCRIPTION OF THE INVENTION

As used herein for description of this invention, the terms E3/6.7K protein and E3/6.7K polypeptide include: a protein or fragment thereof encoded by a nucleic acid as depicted in Figure 1; a Ad2 or Ad5 adenovirus serotype protein or fragment thereof as depicted in Figure 2; or a protein having at least 70% similarity as defined by a Basic Blast search using default parameters to the Ad2 or Ad5 proteins depicted in Figure 2. The Ad5 protein is actually about 7.1K.

Modulation of apoptosis, including inhibition of apoptosis or rescue of a cell from apoptosis may be determined by various methods known in the art, including assays which directly measure apoptosis or which measure the activity of TNF- α , such as those described herein.

Gene Therapy Methods. The isolated nucleic acid molecule depicted in Figure 1, a nucleic acid molecule encoding an E3/6.7K protein as defined herein or a nucleic acid molecule complementary to those described above, may be incorporated into a vector suitable

INTERNATIONAL SEARCH REPORT

International Application No

PCT/CA 00/00663

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/34 C07K14/075 G01N33/68 A61K48/00 A61K39/235

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, CHEM ABS Data, WPI Data, MEDLINE, EMBASE, SCISEARCH

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X A	WO 99 02658 A (SAINT LOUIS UNIVERSITY) 21 January 1999 (1999-01-21) figures 27,28; example 10	8-11 1-5, 12-17
X A	WO 91 08310 A (RES CORP TECHNOLOGIES INC) 13 June 1991 (1991-06-13) page 29, line 3-5; claims 1,2,15,31	8-11 1-5, 12-17
	--- -/--	



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

G document member of the same patent family

Date of the actual completion of the international search

31 October 2000

Date of mailing of the international search report

10/11/2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl.
Fax: (+31-70) 340-3016

Authorized officer

Gurdjian, D

INTERNATIONAL SEARCH REPORT

International Application No

PCT/CA 00/00663

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE DISSERTATION ABSTRACTS 'Online! Dissertation Abstracts Online; AN - 01490827, 1995 LIPPE, ROGER: "MODULATION OF THE MHC CLASS I ANTIGEN PROCESSING AND PRESENTATION PATHWAY" retrieved from DIALOG Database accession no. 01490827 XP002151273	8-11
A	abstract	1-5, 12-17
X	--- ELSING ANDREAS ET AL: "The adenovirus E3/10.4K-14.5k proteins down-modulate the apoptosis receptor Fas/Apo-1 by inducing its internalization." PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES, vol. 95, no. 17, 18 August 1998 (1998-08-18), pages 10072-10077, XP002151270 Aug. 18, 1998 ISSN: 0027-8424	8-11
A	the whole document	1-5, 12-17
X	--- WILSON-RAWLS JEANNE ET AL: "The E3-6.7K protein of adenovirus is an Asn-linked integral membrane glycoprotein localized in the endoplasmic reticulum." VIROLOGY, vol. 195, no. 1, 1993, pages 6-15, XP002151271 ISSN: 0042-6822	8-11
A	cited in the application the whole document	1-5, 12-17
X	--- WILSON-RAWLS JEANNE ET AL: "The signal-anchor domain of adenovirus E3-6.7K, a type III integral membrane protein, can direct adenovirus E3-gp19k, a type I integral membrane protein, into the membrane of the endoplasmic reticulum." VIROLOGY, vol. 201, no. 1, 1994, pages 66-76, XP002151272 ISSN: 0042-6822	8-11
	cited in the application the whole document --- -/--	

INTERNATIONAL SEARCH REPORT

International Application No

PCT/CA 00/00663

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	BRADY H A ET AL: "MAP OF CIS-ACTING SEQUENCES THAT DETERMINE ALTERNATIVE PRE-MRNA PROCESSING IN THE E3 COMPLEX TRANSCRIPTION UNIT OF ADENOVIRUS" JOURNAL OF VIROLOGY, vol. 66, no. 10, 1992, pages 5914-5923, XP000953271	8-11
A	ISSN: 0022-538X abstract -----	1-5, 12-17

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/CA 00/00663

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
WO 9902658	A	21-01-1999	AU	8297098 A	08-02-1999
WO 9108310	A	13-06-1991	AU	6966891 A	26-06-1991
			US	5106965 A	21-04-1992

ATENT COOPERATION TREAT

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 80021-205	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/CA 00/ 00663	International filing date (day/month/year) 07/06/2000	(Earliest) Priority Date (day/month/year) 07/06/1999
Applicant THE UNIVERSITY OF BRITISH COLUMBIA		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 5 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☒ furnished subsequently to this Authority in written form.

☒ furnished subsequently to this Authority in computer readable form.

☒ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☒ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☐ the text is approved as submitted by the applicant.

☒ the text has been established by this Authority to read as follows:

APOPTOSIS INHIBITION BY ADENOVIRUS E3/6.7K

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☒ None of the figures.

INTERNATIONAL SEARCH REPORT

national Application No

PCT/CA 00/00663

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/34 C07K14/075 G01N33/68 A61K48/00 A61K39/235

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, CHEM ABS Data, WPI Data, MEDLINE, EMBASE, SCISEARCH

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X A	WO 99 02658 A (SAINT LOUIS UNIVERSITY) 21 January 1999 (1999-01-21) figures 27,28; example 10 ---	8-11 1-5, 12-17
X A	WO 91 08310 A (RES CORP TECHNOLOGIES INC) 13 June 1991 (1991-06-13) page 29, line 3-5; claims 1,2,15,31 --- -/--	8-11 1-5, 12-17



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

31 October 2000

Date of mailing of the international search report

10/11/2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Gurdjian, D

INTERNATIONAL SEARCH REPORT

International Application No.

PCT/CA 00/00663

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE DISSERTATION ABSTRACTS 'Online! Dissertation Abstracts Online; AN - 01490827, 1995 LIPPE, ROGER: "MODULATION OF THE MHC CLASS I ANTIGEN PROCESSING AND PRESENTATION PATHWAY" retrieved from DIALOG Database accession no. 01490827 XP002151273	8-11
A	abstract	1-5, 12-17
X	--- ELSING ANDREAS ET AL: "The adenovirus E3/10.4K-14.5k proteins down-modulate the apoptosis receptor Fas/Apo-1 by inducing its internalization." PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES, vol. 95, no. 17, 18 August 1998 (1998-08-18), pages 10072-10077, XP002151270 Aug. 18, 1998 ISSN: 0027-8424	8-11
A	the whole document	1-5, 12-17
X	--- WILSON-RAWLS JEANNE ET AL: "The E3-6.7K protein of adenovirus is an Asn-linked integral membrane glycoprotein localized in the endoplasmic reticulum." VIROLOGY, vol. 195, no. 1, 1993, pages 6-15, XP002151271 ISSN: 0042-6822	8-11
A	cited in the application the whole document	1-5, 12-17
X	--- WILSON-RAWLS JEANNE ET AL: "The signal-anchor domain of adenovirus E3-6.7K, a type III integral membrane protein, can direct adenovirus E3-gp19k, a type I integral membrane protein, into the membrane of the endoplasmic reticulum." VIROLOGY, vol. 201, no. 1, 1994, pages 66-76, XP002151272 ISSN: 0042-6822	8-11
	cited in the application the whole document --- -/--	

INTERNATIONAL SEARCH REPORT

International Application No.

PCT/CA 00/00663

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	BRADY H A ET AL: "MAP OF CIS-ACTING SEQUENCES THAT DETERMINE ALTERNATIVE PRE-MRNA PROCESSING IN THE E3 COMPLEX TRANSCRIPTION UNIT OF ADENOVIRUS" JOURNAL OF VIROLOGY, vol. 66, no. 10, 1992, pages 5914-5923, XP000953271	8-11
A	ISSN: 0022-538X abstract -----	1-5, 12-17

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/CA 00/00663

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
WO 9902658	A	21-01-1999	AU	8297098 A	08-02-1999
WO 9108310	A	13-06-1991	AU	6966891 A	26-06-1991
			US	5106965 A	21-04-1992

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
14 December 2000 (14.12.2000)

PCT

(10) International Publication Number
WO 00/75334 A1

(51) International Patent Classification⁷: C12N 15/34,
C07K 14/075, G01N 33/68, A61K 48/00, 39/235

Columbia, St. Paul's Hospital, 1081 Burrard Street, Van-
couver, British Columbia V6Z 1Y8 (CA).

(21) International Application Number: PCT/CA00/00663

(74) Agents: ROBINSON, J., Christopher et al.; Smart &
Biggar, Suite 2200, 650 West Georgia Street, Box 11560,
Vancouver, British Columbia V6B 4N8 (CA).

(22) International Filing Date: 7 June 2000 (07.06.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/137,732 7 June 1999 (07.06.1999) US

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU,
AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE,
DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU,
ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,
LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NZ, NO,
NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR,
TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(71) Applicant (*for all designated States except US*): THE
UNIVERSITY OF BRITISH COLUMBIA [CA/CA];
IRC Room 331, 2194 Health Sciences Mall, Vancouver,
British Columbia V6T 1Z3 (CA).

(84) Designated States (*regional*): ARIPO patent (GH, GM,
KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian
patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European
patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE,
IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG,
CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

(72) Inventors; and

(75) Inventors/Applicants (*for US only*): MOISE, Alexandru,
R. [CA/CA]; Biomedical Research Centre, 2222 Health
Sciences Mall, University of British Columbia, Vancouver,
British Columbia V6T 1Z3 (CA). JEFFERIES, Wilfred,
A. [CA/CA]; Biomedical Research Centre, 2222 Health
Sciences Mall, University of British Columbia, Vancouver,
British Columbia V6T 1Z3 (CA). VITALIS, Timothy, Z.
[CA/CA]; Pulmonary Research Laboratory, Department of
Pathology and Laboratory Medicine, University of British

Published:

- With international search report.
- Before the expiration of the time limit for amending the
claims and to be republished in the event of receipt of
amendments.

For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.

(54) Title: APOPTOSIS INHIBITION BY ADENOVIRUS E3/6.7K

(57) Abstract: This invention provides methods for immune evasion and for evasion of apoptosis by implementing the E3/6.7K protein from adenovirus.

WO 00/75334 A1

INTERNATIC L SEARCH REPORT

Internat Application No

PCT/CA 00/00663

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/34 C07K14/075 G01N33/68 A61K48/00 A61K39/235

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, CHEM ABS Data, WPI Data, MEDLINE, EMBASE, SCISEARCH

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X A	WO 99 02658 A (SAINT LOUIS UNIVERSITY) 21 January 1999 (1999-01-21) figures 27,28; example 10	8-11 1-5, 12-17
X A	WO 91 08310 A (RES CORP TECHNOLOGIES INC) 13 June 1991 (1991-06-13) page 29, line 3-5; claims 1,2,15,31	8-11 1-5, 12-17
	-/--	

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
- *G* document member of the same patent family

Date of the actual completion of the international search

31 October 2000

Date of mailing of the international search report

10/11/2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl.
Fax: (+31-70) 340-3016

Authorized officer

Gurdjian, D

INTERNATIONAL SEARCH REPORT

Int. Application No

PCT/CA 00/00663

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE DISSERTATION ABSTRACTS 'Online! Dissertation Abstracts Online; AN - 01490827, 1995 LIPPE, ROGER: "MODULATION OF THE MHC CLASS I ANTIGEN PROCESSING AND PRESENTATION PATHWAY" retrieved from DIALOG Database accession no. 01490827 XP002151273	8-11
A	abstract	1-5, 12-17
X	--- ELSING ANDREAS ET AL: "The adenovirus E3/10.4K-14.5k proteins down-modulate the apoptosis receptor Fas/Apo-1 by inducing its internalization." PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES, vol. 95, no. 17, 18 August 1998 (1998-08-18), pages 10072-10077, XP002151270 Aug. 18, 1998 ISSN: 0027-8424	8-11
A	the whole document	1-5, 12-17
X	--- WILSON-RAWLS JEANNE ET AL: "The E3-6.7K protein of adenovirus is an Asn-linked integral membrane glycoprotein localized in the endoplasmic reticulum." VIROLOGY, vol. 195, no. 1, 1993, pages 6-15, XP002151271 ISSN: 0042-6822	8-11
A	cited in the application the whole document	1-5, 12-17
X	--- WILSON-RAWLS JEANNE ET AL: "The signal-anchor domain of adenovirus E3-6.7K, a type III integral membrane protein, can direct adenovirus E3-gp19k, a type I integral membrane protein, into the membrane of the endoplasmic reticulum." VIROLOGY, vol. 201, no. 1, 1994, pages 66-76, XP002151272 ISSN: 0042-6822	8-11
	cited in the application the whole document --- -/--	

INTERNATIONAL SEARCH REPORT

Internal Application No

PCT/CA 00/00663

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

[illegible]

INTERNATIONAL SEARCH REPORT

Information on patent family members

Pat. App. No.

PCT/CA 00/00663

Pat. nt document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9902658 A	21-01-1999	AU 8297098 A	08-02-1999
WO 9108310 A	13-06-1991	AU 6966891 A	26-06-1991
		US 5106965 A	21-04-1992